

The Harbeian Oration

ON

THE BIRTH OF CHEMICAL BIOLOGY.

DELIVERED BEFORE THE ROYAL COLLEGE OF PHYSICIANS
OF LONDON, ON OCTOBER 18TH, 1930,

BY

J. B. LEATHES, F.R.C.P., F.R.C.S., F.R.S.,
PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF SHEFFIELD.

WE meet here on St. Luke's Day to honour the wish of William Harvey and to carry out the terms of the deed of gift which he assigned to the College in 1656. Harvey's wish, you remember, was that there should be once every year "a commemoration of all the benefactors of the College," and that this commemoration should keep alive in us the desire "to imitate these benefactors, to contribute our endeavours for the advancement of the society according to their example, and to search and study out the secrets of Nature by way of experiment."

HARVEY'S BENEFACCTIONS.

In any such commemoration we cannot but remember the many ways in which Harvey himself was a benefactor of the College. For fifty years a Fellow, he served as treasurer for many, down to 1629: for forty years he was Lumleian lecturer in anatomy and surgery, to which post he was appointed in 1615; at his own cost he built for the College "a great parlour or convocation house for the Fellows to meet in," with a library and museum above it, which was opened in 1653 with a ceremony sumptuously provided by himself. This hall was built apparently over the court or garden of the premises at Amen Corner, which recently, by the generosity of Dr. Hamey, had been bought for the College. Here, in the year before Harvey's gift, the College had set up his statue.

When Harvey first became a Fellow in 1607, the College meetings were still held at Linacre's house in Knighttrider Street, as they had been since 1518. But in 1614 the rooms at Amen Corner were rented from the Chapter of St. Paul's, and thirty-five years later Dr. Hamey relieved the College of the burden of the annual rent by his purchase and gift. Harvey's hall and library were furnished by him and equipped with books and with instruments at the time, and in his will he left "to the Colledge of Physicians all my bookes and papers and my best Persia long carpet and my blue sattin imbroyed cushion, one paire of brasse Andirons with fire shovell and tongues of brasse for the ornament of the meeting rooms I have erected for that purpose."

But buildings and contents, and the statue of Harvey as well, were destroyed a few years later on the fourth day of the Great Fire. After that the new College buildings in Warwick Lane, built by Wren and Robert Hooke, were not opened till 1674. These buildings served the College for a hundred and fifty years, down to 1825, when the rooms in which we are met came to be identified with the College, as they have now been for three generations. In more than four hundred years there have been but four buildings that have been the College of Physicians. If and when in the fifth century of the life of the College there is to be a fifth, the benefactions of Hamey and of Harvey for the second cannot be forgotten.

But it is not only benefactions such as these that we are bidden to commemorate. Our commemoration is to be of those who have built for all time, who have sought and studied out "the secrets of Nature by way of experiment," and thereby made this College, if they were members, a house of fame, and if not, none the less have deserved well of it. Even in a legal document for the transfer of an estate this single-minded benefactor could not fail to make clear what in his opinion was the

highest claim to commemoration, as his whole life had shown—"the inquiry of truth, which," in the words of his contemporary, "is the lovemaking and the wooing of it."

"DE GENERATIONE ANIMALIUM."

Harvey, you remember, was 50 when he published the *De Motu Cordis et Sanguinis*, and had already been attached to the Court as physician extraordinary to the king for ten years. Four years later he became physician in ordinary to Charles I. Notwithstanding his duties at Court, and his practice both at St. Bartholomew's and among his private patients, and in spite of the political troubles of the times, he continued to make opportunities for pursuing his search into the secrets of nature, amassing materials for the remarkable work which he was at last persuaded to publish in 1651, when he was 73 years old—the *De Generatione Animalium*. "During a long series of years," he tells us there, "for three months in the autumn and winter almost every day I had the opportunity of dissecting numbers of hinds and does" in the royal parks and forests for the study of this subject—not only hunted animals, but also animals set apart for his special use. Week by week the changes are recorded from September on to the end of December. And though perhaps less systematically, he also carried out countless dissections of other viviparous animals during pregnancy. This was in the years before the war; the year 1633 he specially notes as an exceptionally early rutting season.

In 1642, after the battle of Edgehill, he was in Oxford, apparently till its fall in 1646. Of that time Aubrey says: "I remember he came several times to our College (Trinity) to George Bathurst, B.D., who had a hen to hatch eggs in his chamber, which they opened daily to see the way of generation." When Oxford fell, he gave up the wardenship of Merton, to which he had been appointed in the previous year, and returned to London or its neighbourhood. There we know he found that much of his most valued material, on the generation of insects, "the fruits of many years' toil, had not only with the permission but by command of Parliament been abstracted by my enemies from my museum" when his house at the same time was stripped of all its furniture. These notes that perished also must have been collected during the busiest years of his life before the war. He was now 68, and from this time he lived with his brothers, either in London or in its neighbourhood, "finding solace in my studies and a balm for my spirit in the memory of my observations of former years."

The *De Generatione* is therefore remarkable, if only as witness to the single-minded constancy of a busy man "wooing and making love to truth" through half a lifetime. That it profoundly influenced the growth of knowledge, as did the *Opusculum Aureum* of 1628, cannot be maintained. That it is free from "that philosophy of discourse and disputation into which we are betrayed by the forces of our own minds" is too much to say. What work of those days was, if we except the *De Motu Cordis*? But it contains a mass of observation, the result of sustained thought, unwearying anatomical studies, and, as has been so well put before us in recent years by Dr. Herbert Spencer, his watchful attention to a wide clinical experience. Naked-eye anatomy could do no more. It is easy to reflect that it was already possible for the anatomist not to confine himself to naked-eye observations. Harvey used a lens, but the compound microscope had been constructed a good many years before this book appeared. Had the distractions of the times been less cruel it would hardly have been left for Malpighi, fifty years younger than Harvey, to reap the first harvest of microscopic anatomy in the years immediately following Harvey's death. Swammerdam, indeed, made the first observation of blood corpuscles within a year, and the histological publications of Malpighi began with the *De Pulmonibus* three years later. But the microscope has not even now solved the riddles of generation; we can indeed say pretty confidently that it will not. Such was the quest on which Harvey was concentrated for thirty years.

In the seventeenth century modern physiology was born; its birth was attended by two miracles. The first was the miracle of 1628, when Harvey bade medicine take up its

bed and walk, and the delusions of 1,400 years' enslavement to authority and tradition were swept away by the evidence of independent observation and experiment—one of the most remarkable chapters in the history of human thought. The other was the miraculous birth of the physiology of respiration ten years after Harvey's death.

There are passages in the *De Generatione* and the tract on parturition which suggest that Harvey was struggling to emancipate himself from the current doctrines of the functions of the lungs and blood. "Whether the object of respiration is really to cool the animal shall be discussed elsewhere at greater length"; and after giving good reasons for a different account he says:

"If anyone will carefully attend to these circumstances and consider a little more closely the nature of air, he will allow, I think, that air is given neither for the cooling nor the nutrition of animals. It is, as if heat were rather enkindled within the foetus than repressed by the influence of air. Thus much by the way on the subject of respiration; hereafter perhaps I may treat of it at greater length."

But there is no evidence that his own ideas of the nature of air would have furnished the answer to his questionings.

THE BIRTH OF THE PHYSIOLOGY OF RESPIRATION.

He died in 1657. Robert Boyle, who had settled in Oxford three years earlier, was that very year at work with Robert Hooke upon his air-pump. It was completed in 1659. He published his first account of the *New Experiments Physico-Mechanical Touching the Spring of the Air* a year later, and 1661, the date of the second edition, is the date of Boyle's law.

In 1658, a few months after Harvey's death, John Mayow, in his eighteenth year, went as a commoner at Wadham to Oxford, where Boyle had been working for three or four years. Two years later—in 1660—Mayow was elected a Fellow of All Souls, where he studied law and took his bachelor's degree in 1665, after five years. He was, we are told, exempted from taking orders, because he was also studying physic. In 1668 he published his first tract, *De Rachitide*; the following year his second, *De Respiratione*; and in the next year, 1670, he took his doctorate of law.

Mayow's Contribution to Physiology and Chemistry.

The *De Rachitide* is interesting first of all as in it we see how Mayow was saturated with the medicine of his day.* It opens thus:

"There has been only one so far as I know who has written anything on the subject of rickets, namely, the distinguished Dr. Glisson, and that may seem strange, because as a rule disease as it stalks through the land cannot keep pace with the incurable vice of scribbling about it. . . . The disease made its appearance some forty years ago in the western parts of England, and since then has infested infants' cradles through nearly the whole of England, though more rarely the northern part of it."

Now that the causation of rickets is known, it would be an interesting subject for economic and historical research to trace, if this record is true, the cause of the appearance of this disease at that time, and in those parts. He argues that the defective nutrition is not a defect of the blood. Nutrition, according to the ideas of that day, was conveyed also by the nerves. He shared this idea because, he says:

"everyone knows when a nerve is cut not only is sensation lost but nutrition suffers. Moreover when in an experiment on a dog I have accidentally wounded a nerve, on dissection after about three months I have found a fairly conspicuous glandular concretion where the nerve had been cut, and this seemed to have its origin from the nervous juice escaping from the wound of the nerve."

Upon the nature of the contribution of the nerves to nutrition he gives his views in other places. Here he merely says that the nervous juice, meeting and mixing with the blood, produces a certain vigorous reaction and heat ("effervescentiam"). The sections at the end on treatment contain many prescriptions, which for those not familiar with the details of seventeenth century therapeutics are a revelation. The inclusion of 6 drachms of

fresh butter in some of these is an accidental anticipation of modern practice, but it were better that we should not commemorate his advice that it should be administered in an extract *fimi equi non castrati recentis*.

The tract on respiration of 1669 is much more important. The first question he deals with, the entry of air into the lungs, at once shows the school in which he had studied.

"Some," he says, "attribute it to the abhorrence of a vacuum, or some fanciful attraction, others think that the air displaced by the expanding chest pushes adjacent air through the nose and mouth into the lungs, as if the air had an unalterable volume. Whereas if a fairly large bottle with a narrow neck be held to the mouth and the nostrils are closed, air is easily drawn into the lungs through the mouth from the bottle, though the surrounding air cannot be pushing it. The entry of air is effected by its elastic property, so clearly demonstrated by Boyle, and by the pressure of its superjacent air on that which is nearer the surface of the earth. . . . When a bladder squeezed nearly empty of air is tied at the neck and put into a glass from which the air is then pumped out, it is seen to swell, however little air was left in it, as soon as the pressure of the air outside it is removed."

In the second edition of this tract, published five years later, he adds the well-known experiment, more aptly illustrating the entry of air into the lungs, in which the bladder is tied to the inner end of the pipe of a bellows, the valve hole of which has been closed with a glass window; as the blades of the bellows are separated, the bladder can be seen to swell with air, entering it through the pipe, and driven in by the pressure of the atmosphere.

"The structure of the lungs is adapted for their inflation in this way, for they consist, as Malpighi has shown [eight years previously], of a system of most delicate membranes arranged so as to form an almost infinite number of orbicular vesicles communicating so that the air can pass from the trachea into them one after the other and inflate them as the lungs expand."

His description of the enlargement of the chest was in more than one respect for the first time correct, and particularly in that the double articulation of the ribs with the spine, which he was the first to describe in the second edition, 1674, owing to its obliquity when the ribs are raised, causes, not only the sagittal, but also the lateral diameter of the chest to be enlarged. The importance and mode of action of the diaphragm, the significance of orthopnoea, and the small part played by muscular action in ordinary expiration are all clearly set forth.

But it is in the account of the use of respiration that the important revolution appears. The ideas that had been advanced before were three: (1) that the entry of air cooled the blood; (2) that the expansion of the chest drove the blood through the lungs; (3) that the passage of air in and out of the lungs so mixed and agitated the blood that the separation of fluid from solid, known to take place when blood was left to stand at rest outside the body, was prevented.

As to the first of these, he insists that air is necessary for activity and the generation of heat, not for cooling the blood. This is a cardinal fact for him, and is fully developed later. In the first instance, he may have owed this idea to Harvey, as we have seen.

Secondly, the movements of the chest are not necessary for the pulmonary circulation to be carried out, though he recognizes that they help it: blood injected into the pulmonary artery of a dead animal reaches the left ventricle without difficulty, and one has only to hold one's breath and feel one's pulse to recognize that plenty of blood circulates, although the lungs are not moving.

And, finally, that the air does not merely mechanically agitate the blood and so ensure its being properly mixed, as Malpighi maintained in his letter to Borelli, *De Pulmonibus*, 1661, is clear, "since any air however often it had been breathed should be equally effective for this purpose; but air that has been breathed repeatedly cannot maintain life." He quotes, too, "the experiment recently shown at the Royal Society," in which a dog with its chest opened was kept alive by a stream of air driven from a bellows through the trachea, and escaping by punctures at the surface of the lungs. He does not mention that it was shown by Hooke, perhaps because a similar experiment had been done by Vesalius. But Hooke, and Mayow too, realized the importance of the

* Foster mistakenly says that medicine was not Mayow's profession, and that it was law that he practised in the summer at Bath.

experiment as showing that it was not necessary for the lungs to move in order that the animal should live, provided fresh air was supplied. If, with the lungs distended to the same degree, the dog's nose and mouth were closed, it died.

"We may therefore state positively that something absolutely necessary to life is imparted to the blood by the air which is breathed; and when this, whatever it is, is exhausted the air becomes useless and no longer fit for respiration. . . . Expiration has also this further use that in the expelled air certain vapours that exhale from the blood are at the same time blown out."

This last, however, is a point which he did not later attempt to develop.

"What it is in the air that is so necessary for life it is not easy to define. It probably is certain very volatile nitrous particles abundant in the air which are communicated through the lungs to the blood. This aerial nitre is so necessary for every form of life that even plants will not grow in soil deprived of it. Even plants seem to have a kind of respiration and require air."

"What role this aerial nitre plays in animal life is our next inquiry. It appears that when duly mixed with combustible components of the blood it brings about a certain reaction not in the heart alone, but in every muscle that moves—in the heart because it is a muscle, and therefore in its substance rather than in its cavities. For "it is necessary for every movement of the muscles, and without it there could be no movement of the heart; the more violent the movements the more intense and more frequent the respiration, because there is great expenditure of this explosive nitre made necessary by the chemical changes in the contraction of the muscles, and also, in the accelerated action of the heart, which is made necessary by the richer flow of blood to the muscles."

"To this I add that it is proved by the experiments of the most illustrious Boyle that flies, bees, and other insects after being cut through the middle can neither move nor live in a place void of air, though in the air they move for some time. These small animals, therefore, that have neither blood nor hearts nor lungs, at all events in their divided parts, must needs have air it would seem for no other purpose but movement alone."

I have dealt in detail and quoted freely from this first treatise on respiration of 1669 because, while it is short and was written without the fuller development of experimental evidence that is found in the better-known publication of 1674, the position is made clear; the discovery of oxygen, aerial nitre, as a component of the air, and its physiological importance, is clearly outlined. A new planet swims into our ken.

Influence of Boyle and Hooke.

That Boyle had been an inspiration to Mayow is also clear. But there had been other influences. Robert Hooke went up to Christ Church from Westminster in 1653, in the year before that in which Boyle settled in Oxford; he was five years older than Mayow, eight years younger than Boyle. Even at school he had been experimenting with flying machines. He soon attracted the attention of the Warden of Wadham, Dr. Wilkins, who introduced him to Willis, and so to Boyle. Hooke, we know, was working with Boyle at the construction of his air-pump before Mayow went up to Oxford. The *Micrographia* was published by Hooke in 1665, four years earlier than the first *De Respiratione*. In this work "the ingenious Mr. Hooke," as Mayow calls him, had revealed himself in the first place as a born experimenter, a genius, if a rather discursive one. But he had also expressed ideas very similar to those used by Mayow, though in a totally different connexion. He had examined with the microscope the structure of wood charcoal, "an object no less pleasant than instructive," and he proceeds to describe the dry distillation of wood and the part played by air in the process. He speaks of air as a *menstruum* in which combustible materials dissolve with liberation of heat and, if the process is sufficiently energetic, of light.

"This dissolution of combustible bodies is made by a substance inherent and mixt with the air, which is like if not the very same with that which is fixt in saltpeter, which by multitudes of experiments that may be made with saltpeter will, I think, most evidently be demonstrated. Moreover," he adds, "the dissolving parts of the air are but few, and therefore a small parcel of it is quickly glutted and will dissolve no more, and

therefore unless some fresh part of this *menstruum* be apply'd to the body to be dissolved the action ceases and the body leaves to be dissolved and to shine, which is the indication of it, though placed in the greatest heat; whereas saltpeter is a *menstruum* when melted and red hot that abounds more with those dissolvent particles and therefore as a small quantity of it will dissolve a great combustible body so will the dissolution be very quick and violent. Therefore as in other solutions if a copious and quick supply of fresh *menstruum*, though but weak, be poured on or apply'd to the dissoluble body it quickly consumes it. So this *menstruum* of the air if by bellows or any other such contrivance it be copiously apply'd to the shining body is found to dissolve it as soon and as violently as the more strong *menstruum* of melted nitre."

There is so much in this that is entirely new and so much that appears again, *mutatis mutandis*, in Mayow's experiments and arguments that it is clear there must have been intimate communion between the two. Mayow, indeed, has been charged with plagiarism. It would be as fair to make this charge, and perhaps easier to maintain it, against Hooke; he published the ideas first, and Mayow was then 25 and unknown; when Mayow put them out, Hooke was well known and in middle life—not a good subject to play that game on. And as a matter of fact, similar ideas appear in Lower's *De Corde* (Chapter v), published in the same year as the first edition of Mayow's *De Respiratione*. Lower speaks of the nitrous spirit of the air passing into the blood, and states as a dictum "wherever fire can burn with ease we can breathe with ease," a fact established by the experiments described by Mayow. But here, too, there is no attribution to Hooke, nor for that matter to Mayow. But the fact that it was Hooke who proposed Mayow for the Royal Society in 1678 makes it likely that there was no plagiarism, but that Mayow, as a close student and admirer of Boyle, was also intimate with Hooke, and that they worked together, and Lower, too, without stopping to define who had thought first of each experiment or each deduction. That Mayow added nothing is certainly not the case. To begin with, he was a physician and Hooke was not; his first philosophical interest was biology; Hooke was merely incidentally interested in biological science. Gifted with exceptional mechanical ingenuity—when a boy at Westminster he is said to have invented "thirty several ways of flying"—his contribution to science was in the contrivance of experiments of all kinds; as a microscopist he was interested in the structure of charcoal and in explaining why it is black more than in the structure of the living plant. "It is not my design to examine the use and mechanism of these parts of wood, that being more proper to another inquiry," which he leaves alone. He graduates thermometers, but not for physiological experiments. It is in contributions to the technical perfection of the air-pump, and his machine for cutting cogs in clock wheels, that he was at his best. In the preface to his book he says he has "gleaned up here and there a handful of observations in the collection of which I made use of microscopes and some other glasses that improve the sense"; just a discursive miscellany. There, too, he defines his own position in science.

"It is the great prerogative of mankind above other creatures that we are not only able to behold the works of nature, or barely to sustain our lives by them; we have also the power of considering, comparing, altering, assisting and improving them to various uses. By the helps of art and experience some men excel others almost as much as they do beasts. By the addition of such artificial instruments and methods there may be in some manner a reparation made for the mischiefs and imperfections mankind has drawn upon itself by negligence and intemperance and a wilful and superstitious deserting of the prescripts and rules of nature."

As a philosopher his work was typical of the best that the seventeenth century did for experimental science. The remedy for the errors of human reason can only proceed from the substitution of

"the real, the mechanical, the experimental philosophy for the philosophy of discourse and disputation that chiefly aims at the subtilty of its deductions and conclusions without much regard to its first ground work. . . . All the fine dreams and opinions which the luxury of subtil brains has devised would then quickly vanish and give place to solid histories, experiments and works. . . . The links upon which true philosophy depends are to begin

with the hands and eyes, to proceed on through the memory, to be continued by the reason; nor is it to stop there but to come about to the hands and eyes again and so by a continual passage round from one faculty to another it is to be maintained in life and strength as much as the body of a man is by the circulation of the blood through the several parts of the body, the arms, the feet, the lungs, the heart and the head."

He was indeed worthy of a place in the great quartet of Oxford students, who, in the decade following Harvey's death, were led by Boyle; but Boyle was first fiddle, Hooke second, and the subjacent biological ground-tones were supplied by Lower and Mayow.

Mayow did not merely hang himself on. If Boyle and Black and Cavendish are the great names contributed by this country to the creation of physical chemistry, Mayow's is great for the part he played at the birth of biological chemistry, a science to which chemistry owes as much as biology, and without which chemistry would have but three legs to stand on. If the ideas in his work did not all originate with him (the evidence does not make it clear that they did not), by his own experiments he not only established them and made them his own, he extended their implication into fields of thought that meant much less to other members of the team with whom he worked.

The ideas are there in this first edition of the *De Respiratione*, published in 1669, the year after Boyle moved to London. Five years later in the "five tracts" they are extended, enlarged, and the experimental foundations for them given in a way which amply justifies the place that this estimate of his work assigns him.

POSITION OF CHEMISTRY IN THE SEVENTEENTH CENTURY.

It is difficult for us to-day—at first reading I, at any rate, found it impossible—to do justice to Mayow's *De Sal Nitro*, the most important of the five tracts that appeared in 1674, two of which are merely new versions of the earlier ones. When he wrote, hardly any of the terms, hardly any of the ideas which are the alphabet of chemistry, had been defined. The mists and vapours of the Middle Ages obscured everything. It is universally recognized that in order to understand the greatness of what Harvey did, it is imperative to know what had been before; how in the history of human thought Greece and Rome had had to pass away, a new civilization to arise, and after seven centuries also pass away, and yet two centuries more go by before the light shone out that was lit by Harvey. But in that field the Renaissance had then been at work for three generations, even if we disregard all anatomy before Vesalius.

The Renaissance had done nothing for chemistry. Van Helmont, almost exactly Harvey's contemporary, was the only forerunner in the seventeenth century, Paracelsus in the sixteenth, Basil Valentine in the fifteenth. Van Helmont was hardly more clear of mediaeval entanglements than Paracelsus. It is true he weighed the growth of a tree and proved that the increase of weight did not come from the soil. But he concluded that the tree must be made out of water, and argued that the gas into which it was converted when burnt was also transformed water. The "incoercible" gas, "gas sylvestre," given off by fermenting grapes, was no less water. In the six fermentations, which he is at pains to describe, by which food is assimilated to form the living body, there is hardly anything that we can recognize as conforming to fact, as there is nothing that rests upon accurate observation or experiment. Paracelsus or the Arabs themselves could have done as well.

There are but few sidelights on the position of chemistry at the time in England. The sagacious Harvey, we are told, "did not care for chymistry and was wont to speak against the chymists." In a well-known passage, John Wallis, Sedleian professor of geometry, describes the society of philosophers that met weekly in London, from at any rate 1645, out of which the Royal Society arose, and how

"about 1648 some of our company being removed to Oxford our company divided, those in London continued their meetings there, those of us in Oxford did likewise and brought those studies into fashion there, meeting first at Dr. Petty's lodgings, in an apothecary's house because of the convenience of inspecting drugs."

But there were no chemists of the company. Afterwards the meetings were held at Wadham at the lodgings of the warden, Dr. Wilkins, later (some time after 1654) at those of the Honourable Robert Boyle. In 1659, we are told by Anthony Wood, the antiquarian and gossiping historian of Oxford notables, Boyle brought from Strasbourg "the noted chemist and Rosicrucian, Peter Sthael," to lecture in Oxford, and settled him in the house next door to his own lodgings, so that the "elaboratory" which he had there might be convenient for Sthael's use. Sthael apparently lectured for some years; for in 1663 Anthony Wood himself attended. "The club consisted of ten at least"; he mentions names, among them not Mayow's, but "John Lock of Ch. Ch., afterwards a noted writer," also, you remember, a physician.

"This John Lock was a man of a turbulent spirit, clamorous and never contented. The club wrote and took notes from the mouth of their master who sat at the upper end of the table, but the said John Lock scorned to do it so that while every man else would be writing he would be prating and troublesome."

Boyle therefore—one of the inquiring minds who were putting into practice what Bacon had preached—was, unlike Harvey, interested in chemistry. But after the first year of Sthael's course, which he presumably followed, he published, anonymously it is true—no doubt to spare the feelings of his protégé—a destructive criticism of the chemical philosophy of the day, *The Sceptical Chymist*. It should have long been clear that the four elements of the peripatetics could not suffice when experimental chemistry began. But the name of Aristotle kept them in sway, and experimental chemistry had been limited to the action of fire and the use of crucibles and retorts inherited from the alchemists. The empirical chemists since Basil Valentine, who appear to have been seldom great thinkers, had supposed that the properties of different forms of matter depended on the proportions in which the *Tria Prima* occurred in them—volatile mercury, combustible sulphur, and incombustible non-volatile salt. Paracelsus dreamed of a whole system of medicine based on this sort of chemistry. In the *De Origine Morborum ex Tribus Primis Substantiis* he says:

"When you take a bit of wood into your hand your eyes tell you it is a bit of wood, a single substance; that is no use; a rustic can see that. You will see deeper below the surface and know that what you hold in your hand is mercury, sulphur, and salt. It is not till you recognize this that you can be said to see with the eyes of a true physician. He can see this as clearly as the rustic his bit of wood; and what is true of the bit of wood is true of the human body. Whatever burns is sulphur," and he instances resin, gum, turpentine, fat, butter, oil, and strong wine. "Whatever smokes or can be sublimed is mercury, whatever is left as ash is salt."

Bacon commended and adopted this system of the chemists, and in 1622 published the outline sketch of a work he had planned, *Historia Sulphuris Mercurii et Salis*.

Now that people were beginning to use their hands and eyes in the inquiry of truth and to think clearly, it was easy to see that this would not do. But in *The Sceptical Chymist* there is little that is constructive.

Mayow therefore found in chemistry no terms that had been defined, only such as meant one thing at one time and another at another.

"Among the elements of the Peripatetics," he says in the fifth chapter of the *De Sal Nitro*, "the two chief are fire and air. For these two our nitro-aerial mercury [that is, oxygen] might justly be substituted, since it possesses a really fiery nature, and constitutes also the most active part of the air. As to the 'spirit' of the chemists [that is, mercury], which usually heads their array of elements, what they mean by this high-sounding term I simply cannot understand; for the spirits of fermenting liquors which flare up when thrown on the fire should be included in another element of the chemists which they call sulphur [meaning combustible matter]; while the corrosive spirits [spirit of salt, spirit of vitriol, spirit of nitre] should be dealt with among the salts from which they are obtained. If the word spirit is to be retained, it is more appropriate for the nitro-aerial particles in the air, at one time executing motions that are placid, at another the most violent imaginable.

"In the census of the elements sulphur deserves the next place, because after our mercury it is the most fermentative. It, too,

may at one time be sluggish and inert, at another attain full vigour and maturity, or even be untameably wild. From the conflict between these two [or as we should say from the oxidation of organic substances] all the mutations in nature seem to arise."

Then come the salts, which include both the acids and the alkalis, whether fixed or volatile, of which salts in the modern sense are formed. In actual use the term "purely saline salt" means alkaline ash; "acid salt" means the acid component of a neutral salt. Salt of tartar would be potassium carbonate, salt of wormwood the ash of wormwood. "For the rest there is the ubiquitous water and no less ubiquitous Terra damnata," the lifeless earth, dead and damned, that may be left to mineralists.

That is at least a beginning, a scheme that provides a setting for what to Mayow the biologist is the cardinal fact in chemistry, that not only the heart but the whole body lives and moves by the union of oxygen with fuel carried by the blood.

The basal facts upon which he builds are two: first, that in the air there is something which forms only a comparatively small part of it, but which has the same physical properties as the rest, and this it is which is necessary alike for burning and for supporting life; the second, that in nitre this same thing is present, and for this reason combustible matter will burn if mixed with nitre even in the absence of air.

De Sal Nitro.

It is with the second of these themes that he deals first in the opening chapters of the most important of the five tracts, the *De Sal Nitro*. Nitre can be formed in the soil only when air has access to it; the air then contributes something. But the soil certainly contributes something too,

"for nitre is formed in greater abundance in soil impregnated with fixed or volatile salt, as in the neighbourhood of stables, dove-cotes, or slaughter-houses, and also from soil containing quicklime or ashes."

And he knows that when nitre is heated with tartar, the acid spirit of nitre escapes and much more alkaline ash is obtained than is obtained by heating tartar alone, so that nitre contains some fixed salt. This fixed salt is also obtained from nitre when it is heated with oil of vitriol so as to drive off the acid spirit of nitre, the fixed salt being left as the vitriolate, which has all the medicinal and other properties of vitriolate of tartar (potassium sulphate). And similarly, true nitre can be made by neutralizing spirit of nitre with salt of tartar (potassium carbonate). Therefore the fixed salt in nitre certainly is derived from the soil. The other component of nitre, the acid spirit, nitric acid, does not itself exist in the air any more than nitre itself.

"It is probable that the spirit of nitre is a compound and that some of its particles to which it owes its humid and grosser nature are derived from terrestrial matter; others dry and extremely subtle, agile, ethereal and really igneous, these at any rate are certainly derived from air."

The cautious reserve with which this statement is made was justified a hundred years later, when Cavendish showed that both kinds of particles existed in the air and could be made to unite by the passage of electric sparks through it.

The part of nitric acid which according to Mayow's experiments is certainly derived from air is nothing else than oxygen,

"those igneo-aerial particles which are absolutely necessary for the production of flame; let me therefore henceforth call the fiery particles which occur also in air nitro-aerial particles or nitro-aerial spirit."

To account for the other component of nitric acid, the evidence justifies him in concluding that it may be present in what we should call organic matter in the soil, for which the chemists had provided him with no better term than "sulphur"; and the formation of nitric acid from this leads him to a remarkable discussion of the part played by

oxygen in the formation of acids generally, instancing the conversion of iron sulphide by moist air into sulphate from which the acid spirit of vitriol can be obtained; this is also the work of the nitro-aerial particles of the air "much as in the formation of rust or in the souring of ale or wine." If he had only put it into Greek he would have had the word "oxygen," and for the same reasons as those for which Lavoisier gave it this name.

A very important section, also on a purely chemical subject, the mutual affinities of acids and bases, comes later in the treatise (Chapter XIV, "Of the heat of quicklime; incidentally of the combination of contrary salts") and is a clearer exposition of the subject than had yet been given.

"Although acid salts and alkalis pass into a neutral substance when they meet, yet they do not as is generally supposed entirely destroy each other. For example, when the acid spirit of salt is coagulated with sal volatile (and the same is true of sal alkali) although the mixed salts seem to be destroyed, yet they may be separated again with their forces unimpaired. This happens when sal armoniac, or any volatile salt combined with an acid spirit, is distilled with salt of tartar [potassium carbonate]. For then the whole of the acid in the sal armoniac will be coagulated with the fixed salt of tartar, but the volatile salt of which it also in part consists will escape of the same nature as before. And the reason of this is that the acid spirit of salt is prone to enter into closer union with any fixed salt than it is with a volatile salt, so that it immediately leaves the volatile salts to combine more intimately with the fixed salt. If, on the other hand, oil of vitriol be united with salt of tartar they can scarcely be separated from one another, not because they have mutually destroyed one another, but because there is nothing in nature with which either of them can unite more firmly than they do with each other. As acid salts leave volatile salts to form a closer union with the fixed salt of tartar as with a more suitable spouse, so no doubt fixed salts select one acid in preference to another that they may combine with it in a closer union."

The behaviour of nitre with oil of vitriol illustrates this:

"The acid salt of nitre will pass under a mild heat into the receiving vessel, whereas otherwise that spirit will not be carried up except by a very vehement fire. And this is so simply because the acid salt of nitre is volatile and the more fixed vitriolic acid thrusts it from its consort the sal alkali so that it is released from its ties and carried up under the action of no more heat than is necessary for the rectification of spirit of nitre, whereas otherwise it can hardly be divorced from fixed salt unless it be by the most intense heat. The mass left in the retort closely resembles vitriolated tartar, and can fitly be substituted for it."

More follows, as on the combination of metals with acids, on the sulphides of alkalis and metals, and on the theory of incompatibles, that is equally lucid because it rests on orderly experiment done with understanding. The application of the same ideas to the relation of quicklime to slaked lime and the carbonates fails; but nothing better was done with this for eighty years. The experiments are correctly carried out and observed, but without Black's fixed air and the differentiation of mild and caustic alkalis the explanation goes astray.

This work was published when Mayow was 34; he had taken his doctorate in law four years earlier; he was practising medicine at Bath through the summer; his real interest was the physiology of respiration; he apparently did not consider himself ready to take his doctorate of medicine, but he found time to bring order into the chemical thought of the day in the intervals of his other occupations.

The discovery of oxygen—by far the most important step yet taken in the history of chemistry—was of still greater interest in relation to the physiology of respiration. The experimental development of this is in the seventh and eighth chapters of the *De Sal Nitro*.

When a mouse is placed under a bell jar that rests upon a wet bladder stretched over the mouth of a larger vessel the animal as it breathes removes from the air under the jar the component of the air that is taken up in its lungs, and the bladder bulges into the bell jar as the pressure is reduced in it, so that the larger vessel may be lifted bodily by lifting the bell jar. This is precisely similar to what happens when a flame has been burnt in a cupping

glass applied to the skin. Similarly he describes in detail experiments in which he measures the amount of air consumed by a candle burning or by an animal breathing under a cupping glass immersed in water. When the candle goes out and the levels have been duly adjusted the water is found to occupy one-thirtieth of the space previously occupied by air; when the mouse dies, one-fourteenth. In neither case is it possible to kindle in the air that is left combustible matter by means of a burning-glass, as can readily be done in fresh air.

These experiments could not have been done in Harvey's lifetime because the conditions under which alone they could be carried out had not been defined by Boyle. Mayow carried them out with all precaution that could then be devised, and though they suffer from the defect that no account is taken of gaseous products of combustion or respiration, they open an entirely new chapter in the history of both chemistry and physiology. The alembic and crucible no longer constitute the entire armament of the chemist; there is something better for him to do than to go on for ever distilling off mercury from blood and urine.

"Clearly something in the air is absolutely necessary for life and enters the blood in respiration, for if the need for respiration were that the blood may be shaken up and divided into the minute particles by the movement of the lungs the animal should not die so soon, for the air that is left should be able to do this perfectly well; and as it is subject to nearly the whole pressure of the atmosphere there is no reason why it should not enter the expanded chest; for I have shown that it is the pressure of the atmosphere that causes it to do this. It is true the bluntness of our senses prevents us from seeing the passages by which the air enters the blood [just as it prevented Harvey from seeing those by which the blood passed from artery to veins]. They must be exceedingly short and minute, for they merely have to pass through the membranes of the lungs and they must be almost infinite in number. And yet in lungs that have been boiled and dissected an almost infinite number of perforations like the minutest points can be seen with the microscope. Whether they are the mouths of capillary trachea I cannot say.

"Animals and fire draw particles from the air so that it loses elastic force; that these particles are of the same kind in each case is established. If in a similar experiment to those previously described a lamp and a mouse are at the same time enclosed in a glass over water the lamp goes out first and the animal dies later. But the animal dies in about half the time that it would have been able to live had the lamp not been there. It is not suffocated by the smoke of the lamp, for the same result is obtained if spirit of wine is used; moreover I have tried to kindle with a burning glass, in a vessel in which an animal had died from exhaustion of the air, combustible material previously hung in it. I had protected a part of the inside of the vessel from the condensed breath of the animal by a piece of paper which I could pull away by a string passing out below the mouth of the vessel. But it would not take fire. I shall not however make a final statement on this because the season being winter and the sky almost continuously covered with cloud I was not able to repeat the experiment.

"When the lamp goes out or the animal dies the remaining space is filled with air diminished in volume but able to resist the pressure of the surrounding air. I have indeed ascertained that such air is possessed of no less elastic force than any other air, for when the pressure of the atmosphere is removed it expands with no less vigour than common air."

Mayow published nothing after the five tracts. Four years later he was elected to the Royal Society, on Hooke's nomination, left Oxford, and was married, and the following year died in an apothecary's shop off Covent Garden, and was buried in St. Paul's Church there. He was 39—the youngest of the Oxford quartette, and the first to die. The five tracts were translated into Dutch five years later, into German one hundred and twenty years later, in 1799, into French in 1840, and into English in 1807.

The only reference to his work for more than one hundred years after his death appears to have been made by Stephen Hales. His work was forgotten. His discoveries rediscovered were the starting point of modern chemistry. By that time men's minds had become ground in which the seed could germinate.

You will, I hope, think that in our commemoration it is fitting that he should be remembered in the twentieth century, if only because he was so sadly forgotten in the eighteenth.

ANAESTHESIA FOR OPERATIONS UPON THE GRAVID UTERUS.*

BY

H. W. FEATHERSTONE, M.D.,

HONORARY ANAESTHETIST, GENERAL HOSPITAL, AND MATERNITY
HOSPITAL, BIRMINGHAM.

It is the intention of this paper to show how, by a wise selection of methods, the anaesthetist may collaborate with the obstetric surgeon to make his work more effective and the safety of the patient more secure.

Preliminary Considerations.—During pregnancy women tolerate anaesthetic drugs exceedingly well. Last year, at the Birmingham Maternity Hospital, nitrous oxide was administered to more than three hundred women for dental extractions at all stages of pregnancy, and there was not a single miscarriage. Ether, chloroform, gas-oxygen, and spinal anaesthetics are often administered for all kinds of surgical procedures, but, save in the presence of dangerous infections, such as peritonitis, it is rare for the pregnancy to be interfered with.

Operations on the uterus and its appendages, when in the gravid state, fall into three groups: (1) operations only on the uterus and its appendages; (2) operations on the uterine contents; and (3) operations on the gravid uterus together with its contents.

OPERATIONS ONLY ON THE UTERUS AND ITS APPENDAGES.

These operations are usually undertaken with the purpose of improving the course of the pregnancy, or of making normal and unobstructed labour possible; thus it may be necessary in the earlier months of pregnancy to replace a retroverted gravid uterus. Inasmuch as muscular relaxation of the abdominal wall is required, and cyanosis is not advisable, ether preceded by atropine is more satisfactory than gas or gas-oxygen.

Fibroid tumours (particularly those in the cervix) and simple ovarian cysts may obstruct the pelvic cavity; removal of these is often a matter of considerable operative difficulty. The aims of the anaesthetist are therefore abdominal relaxation, the avoidance of circulatory congestion and oozing from cyanosis, and the least possible disturbance of the kidney and liver functions. Perhaps the best compromise is obtained with chloroform, or a mixture of chloroform with ether. Gas-oxygen does not give sufficient relaxation, and the resulting tension and pressure on the uterus may produce an intrauterine haematoma, resulting in a miscarriage. Spinal analgesia is useful because it controls the bleeding.

Mr. Lewis Graham of Birmingham has permitted me to quote a series of six operations for myomectomy which were performed under a mixture of chloroform and ether without any untoward event. In one instance the fibroid was as large as a coco-nut and deeply embedded. After removal, the base of the placenta could be seen at the bottom of the wound in the uterine wall, but the pregnancy continued normally. By way of contrast, however, I may refer to a case, at the sixth month of gestation, in which an adherent degenerating fibroid was removed, under ether, with very great difficulty; the woman miscarried on the next day.

Accidents to ovarian tumours, such as rotation or infection, may render the patient acutely ill; in these cases the anaesthetist must help the surgeon to save the patient's life regardless of the pregnancy. Gas-oxygen is a very suitable agent, because anaesthetic toxæmia and post-operative collapse are reduced to the minimum. Indeed, relaxation in these conditions is obtained with comparative ease. Ruptured ectopic gestation is usually best dealt with under gas and oxygen. But in a case of ruptured tubal gestation, which was complicated by severe bronchopneumonia, a spinal anaesthetic was employed with a satisfactory result.

*A paper read in opening a discussion in the Section of Anaesthesia at the Annual Meeting of the British Medical Association, Winnipeg, 1930.